Measurement error problems in image co-registration: a prostate cancer investigation

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Outline

- Prostate Cancer Investigation Team
- Study Procedure
- Co-Registration Procedure
- Measurement Error in Co-Registration
- Statistical Consideration

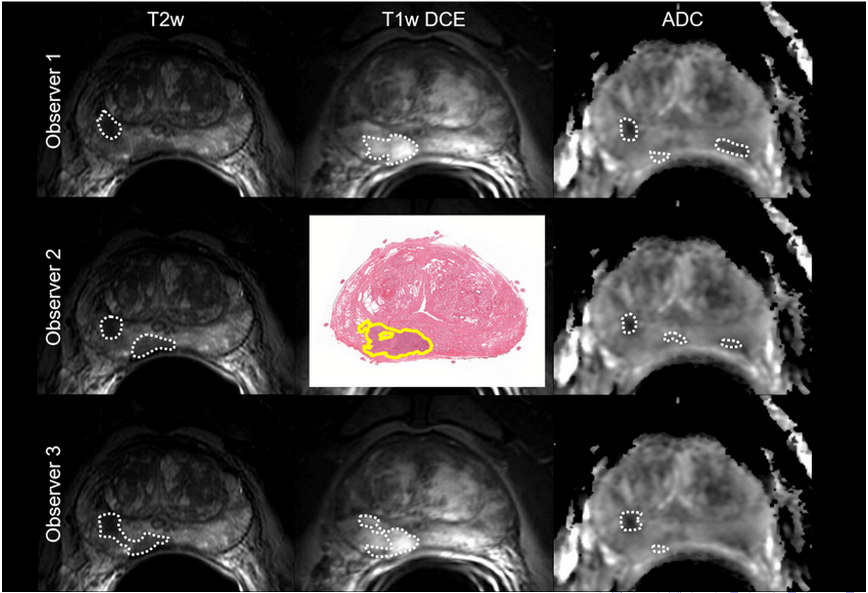
Prostate Cancer Research Team Project

- Started from 2008, Team in Image-Guided Prostate Cancer Management.
- Canadian Institute of Health Research (CIHR) support: initial 5 million
- Involvement
  - University of Western Ontario (UWO)
  - Robarts Research Institute
  - Lawson Health Research Institute (LHRI)
  - London Health Research Center (LHRC)
  - London Cancer Research Program (LCRP)
  - Victoria Hospital in London
  - St. Joseph Hospital in London
  - Sunnybrook Hospital in Toronto

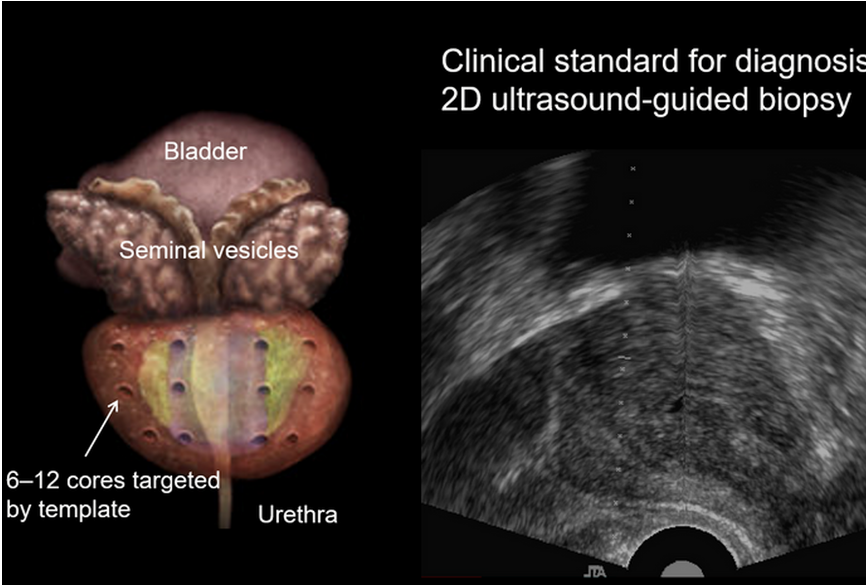
Prostate Cancer Research Team Project

- Team:
  - Imaging Physicists
  - Medical Imaging Scientists
  - Oncologists
  - Pathologists
  - Urologists
  - Biostatisticians
- Imaging techniques
  - MRI (T2w, T1w DCE, DWI, PET, Sodium)
  - CT-perfusion
  - 3D UltraSound

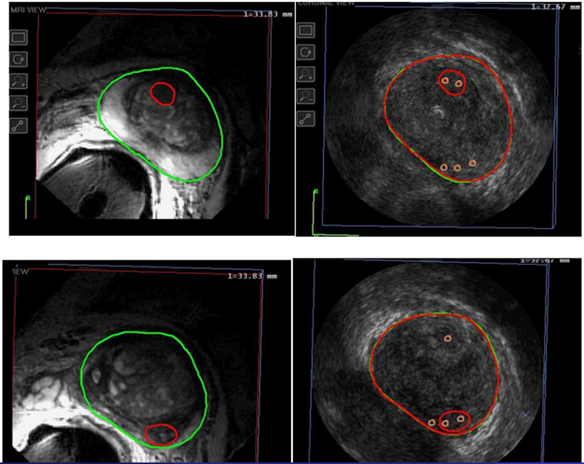
Standard Diagnosis: cancer contour



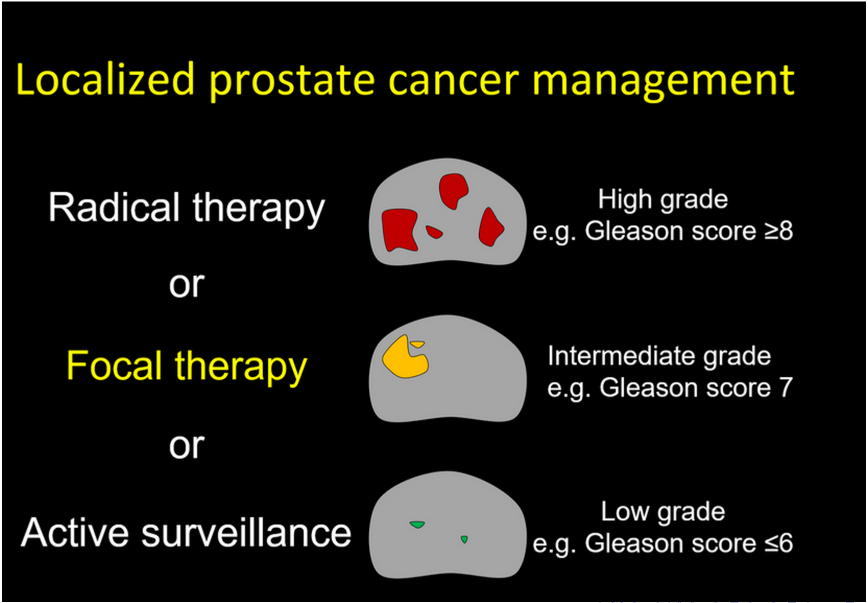
Standard Diagnosis: biopsy confirmation



3D registration of a planning MRI to 3D TRUS can define biopsy target regions in the 3D TRUS context.



Standard: Treatments



Project Objectives

Primary Objectives

- Accurate diagnosis of prostate cancer: stage, volume, position
- Accurate confirmation of cancer: image guided biopsy
- Targeted treatment: focal therapy

Goals of the Study

- Divide the prostate into voxels (about 4 mm^3 per unit)
- Prediction of cancer at each voxel in the prostate
- Derive the diagnostic features based on the prediction
- Target biopsy needle and focal treatment to the exact position of cancer

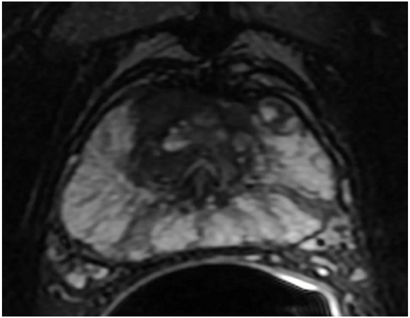
Study procedure

- Pre-operative imaging: mpMRI (T2w, T1w DCE, DWI), CT-perfusion, 18FCH PET MRI, 3D RF time series ultrasound (in vivo)
- Prostatectomy operation
- Slice the prostate, take histological digital image and pathologists contour the cancer on the image (post-op whole mount histology at $0.5\mu m$ per pixel)
- Align the information of imaging data and digital histology data for each voxel

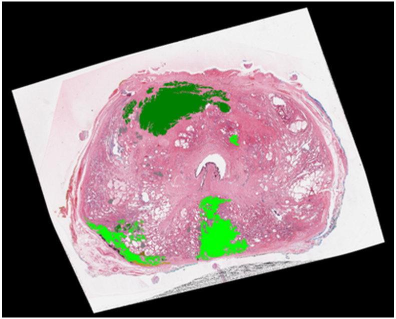
Challenge:

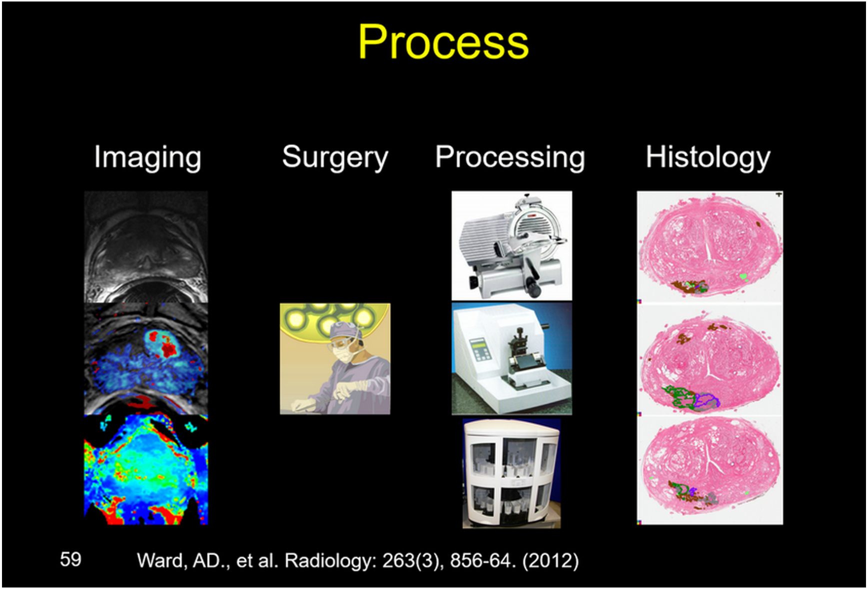
Co-registration of in vivo imaging data with digital histology

T2W MRI

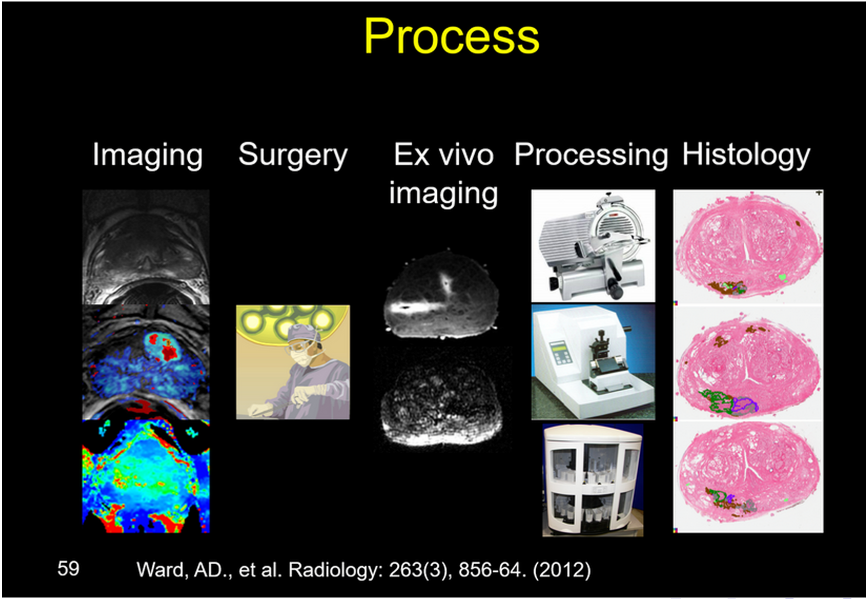


Digital Histology

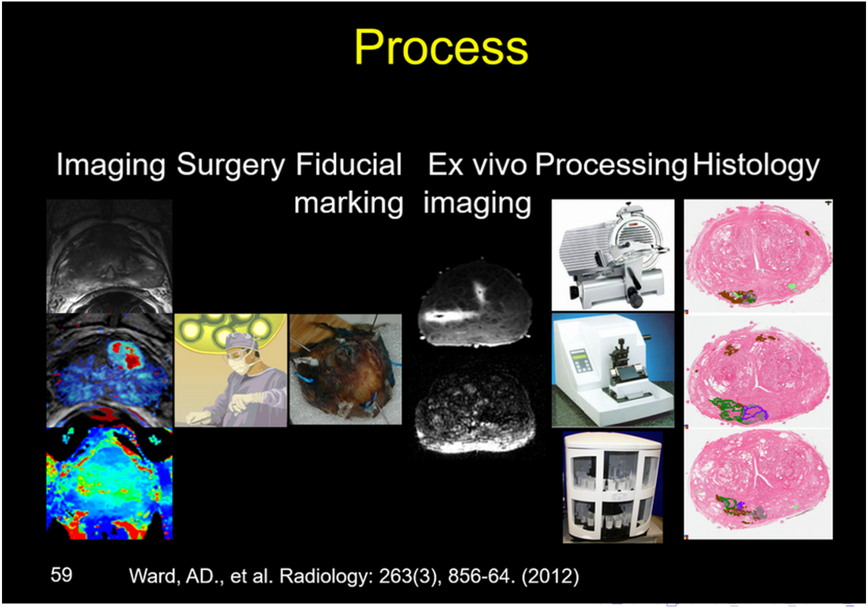


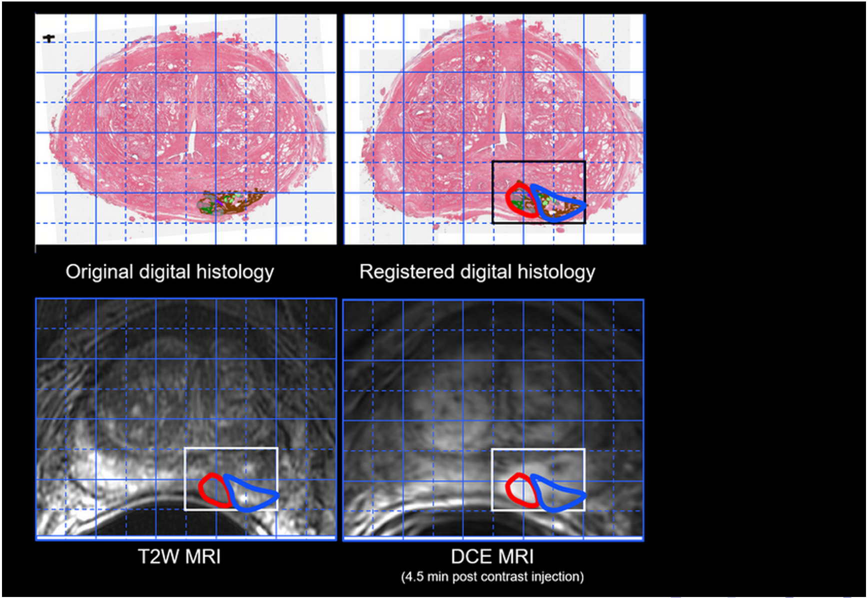

Process
Imaging
Surgery
Processing
Histology
59
Ward, AD., et al. Radiology: 263(3), 856-64. (2012)

Registration



Registration




Original digital histology
Registered digital histology
T2W MRI
DCE MRI
(4.5 min post contrast injection)

3D registration of ex vivo prostate digital histology to in vivo mpMRI

The procedure of in vivo MRI and ex vivo histology Co-Registration

- After prostatectomy, fiducial will be insert in the prostate, and an ex vivo MRI image is then taken
- The prostate is then sliced and the histology digital image is taken for each slice of prostate
- The ex vivo MRI is aligned with the in vivo MRI: automatical plus manual adjustment
- The histology image is aligned with the ex vivo MRI slices: the fiducial is used for reference
- Create the correspondence of in vivo MRI image with the histology image
- Other in vivo images, like CT, PET/MRI, will be aligned with the in vivo MRI, and make connection with histology image.

Errors introduced in all of the steps!

Errors include:

- Deformation due to endorectal receive coil
- Formalin fixation
- Histoprocessing
- Variability in cutting orientation
- Variability in cancer contouring

Co-Registration: Error

Registration error

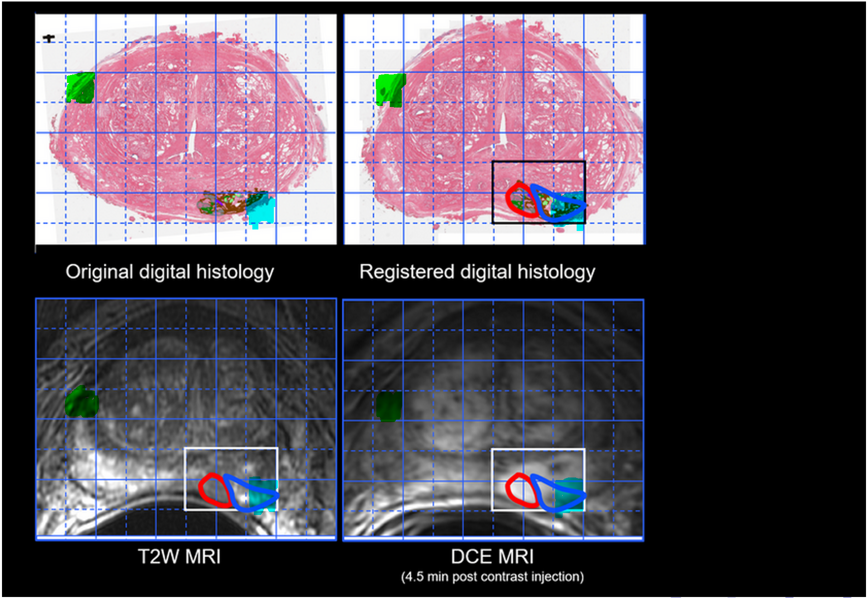
Overall histology-to-mpMRI 3D registration error: 1–2 mm

Registration stage	**Mean ± std 3D registration error (mm)**
3D histology reconstruction to ex vivo MRI	0.7 ± 0.4
Ex vivo MRI to in vivo high-res 3D T2W MRI	1.4 ± 0.2
High-res 3D T2W MRI to clinical mpMRI	0.7 ± 0.1 (T2W)
	1.0 ± 0.5 (DCE)
	1.0 ± 0.2 (ADC)

Data

- $\mathbf{X}_{ijkl}$: imaging data for each of the voxels, in vivo. j, k, l are 3-D coordinates
  - Intensities for mpMRI
  - Blood flow, blood volume etc. for CT
  - Intensities for 3D UltraSound
- Y^*_{ijkl}: histology digital data: percentage of cancer in each voxel or binary cancer/no cancer status, ex vivo
- Y_{ijkl}: in vivo cancer status, unknown
- Building the correspondence of Y^*_{ijkl} and $\mathbf{X}_{ijkl}$: co-registration by biomedical engineer.

Data


Original digital histology
Registered digital histology
T2W MRI
DCE MRI
(4.5 min post contrast injection)

Statistical Goal

Statistical predictive models of true cancer status Y_{ijkl} using imaging data variables $\mathbf{X}_{ijkl}$ is of primary interest.

- Logistic Regression:

$$\text{logit} Pr(Y_{ijkl} = 1) = \beta \mathbf{X}_{ijkl}$$

- Regression Tree
- Random Forest
- Support Vector Machine
- Adaptive Support Vector Machine

Statistical Challenges

- True Y_{ijkl} unknown
- Using $\{\mathbf{X}_{ijkl}, Y^*_{ijkl}\}$ from the co-registration to train the predictive model

$$Y^*_{ijkl} = h(\mathbf{X}_{ijkl})$$

- AUCs

Model	AUC	7-fold CV-AUC
Logistic Regression	0.692	
Regression Tree	0.809	0.832
SVM	0.733	
Adaptive SVM	0.914	0.916

- The predictive model $Y^*_{ijkl} = h(\mathbf{X}_{ijkl})$ can be used for diagnosis purpose, to calculate volume, stage, etc. based on $\hat{Y}^*_{ijkl}$.
- This won't work for guiding biopsy and treatment: we need the exact in vivo position of the cancer: $\hat{Y}_{ijkl} =?$
- Question: How can we build relationship between Y^*_{ijkl} and Y_{ijkl}, thus $\hat{Y}^*_{ijkl}$ and $\hat{Y}_{ijkl}$

Statistical Challenges

Use the "validation data" to estimate

$$\Pr(Y_{ijkl} = 1 | Y^*_{ijkl}, \mathbf{X}_{ijkl})$$

"Validation Data": Majority voxels do not have cancer, and some voxels do have cancer for sure

Correlation Consideration

- All cancer status Y_{ijkl} come from the same prostate of an individual : j, k, l are the 3-D position coordinates. They are correlated
- The correlation may be high for the adjacent voxels
- Because of the co-registration, observations are Y^*_{ijkl} are the surrogates of Y_{ijkl}
- For prediction, any way to make use of association among Y_{ijkl} indexed by position (j, k, l) for the relationship between Y^*_{ijkl} and Y_{ijkl}
- Question: can we make use of the association to find the true Y_{ijkl}

Suggestions and Comments?